Separating People from Pollution

Individual and Community Interventions to Mitigate Health Effects of Air Pollutants

Efforts to minimize people's exposure to air pollution historically have focused on curbing emissions from tailpipes and smokestacks. But increases in vehicle-kilometers traveled—that is, more cars spending more time on the road—have tempered that effect. Moreover, residential areas, hospitals, and schools often are built adjacent to main traffic arteries, where emissions are highest. An international group of public health researchers now says it's time to start separating people from sources of air pollution as a means of protecting public health [***EHP* 119(1):29–36; Giles et al.**].

Air pollution can cause myriad cardiovascular and respiratory problems including asthma, bronchitis, and heart disease. Outdoor air pollutants can easily migrate indoors, and most exposure to ambient air pollution occurs inside buildings. Recent research indicates that people living near congested highways face a greater risk of such diseases and that moving to a less-polluted neighborhood lowers their risk.

The authors describe "promising and largely unexplored" approaches to reducing the health impact of air pollution through interventions targeted at communities and at individuals. They base their recommendations on published studies and discussions from a 2009 workshop on this topic held in Vancouver, Canada.

The authors argue that cities can improve residents' health by considering air quality during land-use planning. For example, creating high-density, mixed-use areas would enable more people to walk or bicycle to work, school, and shops, thereby reducing emissions and encouraging more exercise; ideally, safe pedestrian and cycling greenways would be located away from traffic. For longer-distance travel, the authors suggest low-emission public transit. And in areas where wood burning is an important heating method, woodstove exchange programs can help residents acquire cleaner-burning stoves affordably.

Time of day and location affect air pollution exposure during exercise.

Risk factors for heart disease include a sedentary lifestyle, obesity, and a high-sodium diet. Therefore, the authors posit that another approach to reducing a person's risk of being affected by air pollution is to minimize one's overall risk of heart disease. This could involve interventions that encourage people to eat a diet rich in omega-3 fatty acids and antioxidants and to get regular exercise. However, because pollution levels vary even within cities, exercise should be planned to minimize exposure. Variations occur by season, with ozone being higher in the summer and particulates from woodstoves higher in the winter, for example. Traffic-related pollutants also spike during rush hour and are higher in heavily traveled areas.

Cynthia Washam writes for *EHP*, *Oncology Times*, and other science and medical publications from South Florida.

Estrogens from the Outside In

Alkylphenols, BPA Disrupt ERK Signaling *in Vitro*

The body produces estrogens—including estrone (E_1), estradiol (E_2), and estriol (E_3)—that direct reproductive system processes and contribute to the normal function of tissues including the brain, bone, and cardiovascular system. Certain xenoestrogens (estrogenic compounds introduced from outside the body) are suspected of disrupting these activities. In a new study, xenoestrogenic alkylphenols and bisphenol A (BPA) interfered with normal estrogenic signaling *in vitro*, which suggests they could disrupt normal physiologic function at critical life stages [***EHP* 119(1):104–112; Jeng and Watson**].

Different estrogen receptors control different functions: receptors in the cell nucleus direct gene transcription, whereas receptors in the cell membrane direct signaling pathways via extracellular signal–regulated kinases (ERKs). ERK-controlled pathways respond to many biochemical stimuli and integrate these signals to direct a cell toward division, differentiation, death, or malignant transformation. The structurally related alkylphenols and BPA interact weakly with nuclear estrogen receptors, but they can have pronounced effects on signaling pathways mediated by estrogen receptors in the cell membrane.

In the current study, a rat pituitary cancer cell line was used to study the effect of alkylphenols and BPA on ERK1 and ERK2 activation (measured as phosphorylation), both alone and in combination with each physiologic estrogen. After treatment with each physiologic and environmental estrogen, the researchers measured time-dependent surges in ERK activation. In most cases, E_1 and E_2 prompted early, intermediate, and late surges in ERK activation at 5, 10–30, and > 30 min, respectively; alkylphenols and E_3 typically triggered early and late surges. Interestingly, a very low concentration of BPA (10^{-14} M) yielded a similar two-peak response, but a higher concentration (1 nM) induced a three-peak response like that of E_1 and E_2. Both BPA concentrations were typical of environmental exposures and, along with ineffective midrange doses, also illustrated the nonmonotonic dose–response relationship characteristic of many estrogenic compounds.

When physiologic estrogens and xenoestrogens were combined, the response pattern generally shifted to a single major peak at an intermediate time. Xenoestrogens that caused a strong response when administered alone at a particular point in time or concentration tended to inhibit ERK activation in response to a physiologic estrogen. But at other times or concentrations, the same xenoestrogen might cause a weak response on its own, in which case it would tend to enhance ERK phosphorylation in response to physiologic estrogens.

There were exceptions to these general patterns, however, which highlights the need to study effects of individual xenoestrogens at different points in time, at varying concentrations, and in different tissues. The effect of shifts in the patterns of ERK activation are only just beginning to be explored, although it is known that these patterns constitute an important component of information flow within a cell. The correct flow of information is likely to be especially critical during windows of vulnerability that are based in part on life stage.

Julia R. Barrett, MS, ELS, a Madison, WI–based science writer and editor, has written for *EHP* since 1996. She is a member of the National Association of Science Writers and the Board of Editors in the Life Sciences.

A Measure of Community Exposure

PFOA in Well Water Correlates with Serum Levels

The first detailed investigation into contamination of private wells with perfluorooctanoic acid (PFOA) and levels of the compound in human blood serum suggests that drinking water was the dominant source of exposure to PFOA in a community industrially exposed to the compound [***EHP* 119(1):92–97; Hoffman et al.**]. The study, conducted in 2005 and 2006, included only people who obtained their drinking water from private wells. The results showed that each 1-µg/L increase of the compound in the participants' water supply was associated with a 141.5-µg/L increase in people's serum PFOA concentrations.

The participants lived around DuPont's Washington Works facility in Parkersburg, West Virginia, where PFOA (also known as C8) is used in the manufacture of Teflon® nonstick polymers. PFOA has been shown to increase risk of cancer, reproductive problems, and liver damage in laboratory animals, although human health effects are less clear. Many of the water monitoring data used in this study were collected as part of an agreement between DuPont and the U.S. Environmental Protection Agency (EPA) to conduct a human health risk assessment for PFOA.

The groundwater in the Parkersburg area had been contaminated by DuPont's releases of PFOA into the nearby Ohio River. A second source of contamination was PFOA that was released into the atmosphere and deposited onto soils, which then leached into the groundwater.

Previous research in this study area linked drinking water supplied by six local water districts and consumption of home-grown vegetables to PFOA levels in participants' serum [*EHP* 118(8):1100–1108; Steenland et al.]. The new study provides a quantitative estimate of the relationship between drinking water and serum PFOA levels based on exposure to a wider range of PFOA levels in drinking water from 62 wells. It also corroborates the earlier finding about consumption of home-grown vegetables.

Many of the wells in the study had PFOA concentrations that exceeded the EPA's 0.4-µg/L advisory level, although the median concentration in the well water samples was half that level. The concentrations of PFOA in participants' serum ranged from 0.9 to 4,751 µg/L, with a median of 75.7 µg/L, approximately 20 times the average level in the U.S. general population.

The association between PFOA in drinking water and serum was similar for both shorter- and longer-term residents of the area. The researchers found the associations held after excluding participants who reported drinking bottled water and those who worked at the DuPont facility. Compared with other factors (including age, sex, body weight, cigarette smoking, and alcohol consumption), drinking water was consistently the strongest predictor of serum PFOA levels.

The 141.5:1 ratio estimated for drinking water to serum PFOA concentrations is close to the 114:1 ratio predicted by a steady-state pharmacokinetic model employed by the authors. These findings may be useful in developing drinking water guidelines and studying other communities where PFOA is manufactured.

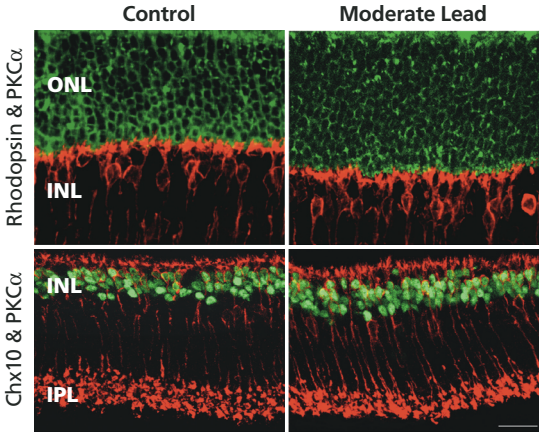
Kellyn S. Betts has written about environmental contaminants, hazards, and technology for solving environmental problems for publications including *EHP* and *Environmental Science & Technology* for more than a dozen years.

Lead Doesn't Spare the Rod

Low-Level Exposure Supercharges Retinal Cell Production in Mice

Low-level gestational lead exposure has been shown to increase the electrical response of the rod signaling pathway in the retinas of children, monkeys, and rats, which could in turn contribute to retinal disease. Now researchers demonstrate the phenomenon underlying this effect: increased proliferation of retinal progenitor cells, which give rise to functionally differentiated retinal cells that sense and transmit visual information [***EHP* 119(1):71–77; Giddabasappa et al.**].

Using a previously described mouse model of low-level gestational lead exposure, the researchers set out to test the hypothesis that such exposure selectively increases rod photoreceptors and bipolar cells in the rod signaling pathway. (The rod signaling pathway detects gradations of light, as opposed to the cone signaling pathways, which detect colors.) Female mice were given water containing varying concentrations of lead: 0 ppm (control), 27 ppm ("low" dose), 55 ppm ("moderate" dose), or 109 ppm ("high" dose). The exposures were administered for 2 weeks before mating, during pregnancy, and through postnatal day 10—a model for the human gestation period. On postnatal day 10, unspiked water replaced the water–lead mixtures for all groups.



Rhodopsin = rod nuclei; PKCα = rod bipolar cells; Chx10 = rod and cone bipolar cell nuclei; ONL = outer nuclear layer; INL = inner nuclear layer; IPL = inner plexiform layer; scale bar = 20 µm

The retina comprises several layers; among them, the ONL is composed of rod and cone nuclei, while the INL is composed of bipolar cells that transmit signals from the rods and cones to retinal nerve cells as well as numerous other cell types. Gestational lead exposure selectively increased the number of rods and bipolar cells.

Donald A. Fox

The adult mammalian retina consists of six types of neurons and a Müller glial cell. These cell types develop in one of two distinct phases: primarily *in utero* ("early-born") or primarily after birth ("late-born"). In examining controls and exposed mice at postnatal day 60, the researchers found that late-born rod photoreceptors and rod and cone bipolar cells increased by 16–30% in exposed offspring, whereas Müller glial cells (also classified as late-born retinal cells) did not increase. Low and moderate lead doses showed the greatest effects. Gestational lead exposure also increased and prolonged retinal progenitor cell proliferation but did not alter developmental apoptosis (programmed cell death), indicating that the higher numbers of rods and bipolar cells were due to increased production, not decreased apoptosis.

These results demonstrate that gestational lead exposure resulting in blood lead levels of 10 µg/dL alters retinal development by selectively promoting the development of rod photoreceptor cells and bipolar cells. The authors speculate that the increased number of rods and bipolar cells in the lead-exposed animals could accelerate age-related retinal degeneration. These nonmonotonic dose–response results raise complex issues for neurotoxicology, risk assessment, public health, and children's health.

Angela Spivey writes from North Carolina about science, medicine, and higher education. She has written for *EHP* since 2001 and is a member of the National Association of Science Writers.